Alternative splicing in the differentiation of human embryonic stem cells into cardiac precursors.

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Public Summary:
The role of alternative splicing in self-renewal, pluripotency and tissue lineage specification of human embryonic stem cells (hESCs) is largely unknown. To better define these regulatory cues, we modified the H9 hESC line to allow selection of pluripotent hESCs by neomycin resistance and cardiac progenitors by puromycin resistance. Exon-level microarray expression data from undifferentiated hESCs and cardiac and neural precursors were used to identify splice isoforms with cardiac-restricted or common cardiac/neural differentiation expression patterns. Splice events for these groups corresponded to the pathways of cytoskeletal remodeling, RNA splicing, muscle specification, and cell cycle checkpoint control as well as genes with serine/threonine kinase and helicase activity. Using a new program named AltAnalyze (http://www.AltAnalyze.org), we identified novel changes in protein domain and microRNA binding site architecture that were predicted to affect protein function and expression. These included an enrichment of splice isoforms that oppose cell-cycle arrest in hESCs and that promote calcium signaling and cardiac development in cardiac precursors. By combining genome-wide predictions of alternative splicing with new functional annotations, our data suggest potential mechanisms that may influence lineage commitment and hESC maintenance at the level of specific splice isoforms and microRNA regulation.

Scientific Abstract:
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